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Ambient Water Quality Criteria: Trichloroethylene

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Section 304(a) of the Clean Water Act (33 U.S.C. 1314(a)), requires EPA to publish and periodically update water quality criteria. These criteria are to reflect the latest scientific knowledge on the identifiable effects of pollutants on public health and welfare, aquatic life, and recreation. This report presents water quality criteria for trichloroethylene. It presents concentration criteria for the protection of fresh water and saltwater aquatic life. It presents 'safe' concentrations for humans, and in the case of suspect or proven carcinogens, gives various levels of incremental cancer risk. A section 304(a) water quality criterion is a qualitative or quantitative estimate of the concentration of a water constituent or pollutant in ambient waters which, when not exceeded, will ensure a water quality sufficient to protect a specified water use. Under the Act a criterion is a scientific entity, based solely on data and scientific judgment. It does not reflect considerations of economic or technological feasibility nor is it a water quality standard and in itsel, ...

KEYWORDS: *Water quality, *Toxicology, *Water pollution effects(Humans), *Water pollution effects(Animals), *Toxic substances, *Ethylene/trichloro.

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PB 292443

TRICHLOROETHYLENE

Ambient Water Quality Criteria

Criteria and Standards Division
Office of Water Planning and Standards
U.S. Environmental Protection Agency
Washington, D.C.

CRITERION DOCUMENT

TRICHLOROETHYLENE

Criteria

Aquatic Life

For trichloroethylene the criterion to protect freshwater aquatic life (as derived using the Guidelines), is 1,500 µg/l as a 24-hour average and the concentration should not exceed 3,400 µg/l at any time.

For saltwater aquatic life, no criterion for trichloroethylene can be derived using the Guidelines, and there are insufficient data to estimate a criterion using other procedures.

Human Health

For the maximum protection of human health from the potential carcinogenic effects of exposure to trichloroethylene through ingestion of water and contaminated aquatic organisms, the ambient water concentration is zero. Concentrations of trichloroethylene estimated to result in additional lifetime cancer risks ranging from no additional risk to an additional risk of 1 in 100,000 are presented in the Criterion Formulation section of this document. The Agency is considering setting criteria at an interim target risk level in the range of 10^{-5}, 10^{-6}, or 10^{-7} with corresponding criteria of 21 µg/l, 2.1 ug/l, and 0.21 µg/l, respectively.

Introduction

Trichloroethylene (1,1,2-trichloroethylene; TCE) is a clear colorless liquid, characterized by the formula C_2HCl_3. It is used mainly as a degreasing solvent in metal industries. TCE also has been used as a household and industrial drycleaning solvent, an extractive solvent in foods, and as an inhalation anesthetic during certain short-term surgical procedures (Huff, 1971).

TCE has a molecular weight of 131.4; a water solubility of 1,000 µg/ml; a vapor pressure of 77 mm Hg and a melting point of 83 degrees C (Patty, 1963). The experimentally determined logarithm of the octanol/water partition coefficient (log P) for TCE is 2.29, which indicates that it may bioaccumulate (Radding, et al. 1977). Its relative chemical stability, non-flammability, volatility and poor water solubility make TCE a very useful solvent.

Annual production of TCE in the United States approximates 234,000 metric tons (40 FR 48907-Oct., 1975). The volatilization of TCE during production and use is the major source of environmental levels of this compound. TCE has been detected in air, in food, and in human tissues (Pearson and McConnell, 1975). Its detection in rivers, municipal water supplies, the sea, and aquatic organisms indicate that TCE is widely distributed in the aquatic environment. (McConnell, et al. 1975; Pearson and McConnell, 1975; U.S. EPA, 1978a).

TCE is not expected to persist in the environment because of its rapid photooxidation in air, its low water solubility and its volatility (Pearson and McConnell, 1975; Dillings, et al. 1976; Patty, 1963). The most serious known exposures of humans to TCE occur in the industrial populations that manufacture or use the compound (NIOSH, 1973).

Under laboratory conditions, TCE has been shown to be toxic to fish (Alexander, et al. in press; Pearson and McConnell, 1975; U.S. EPA, 1978b). The acute toxicity of TCE in mammals is manifested primarily by depression of the central nervous system (Stewart, et al. 1970). In addition to the neurological effects in humans and experimental animals, TCE produces liver damage. Severe and persistent toxicity to the liver was recently demonstrated when TCE was shown to produce carcinoma of the liver in mouse strain B6C3F1 (NCI, 1976). This finding has created additional concern about the toxicity of TCE.

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AQUATIC LIFE TOXICOLOGY*

FRESHWATER ORGANISMS

Introduction

No data on the effects of trichloroethylene on freshwater aquatic life were published prior to 1978, and consequently, the data base is quite limited.

Acute Toxicity

Alexander, et al. (1978) tested fathead minnows in flow-through tests with measured concentrations and in static tests without measuring the exposure concentrations. Although LC50 values of 40,700 and 66,800 µg/l, respectively, were obtained for the same species, when the static LC50 is adjusted for test conditions according to the Guideline procedures, the adjusted static LC50 value is 36,500 µg/l as compared to 40,700 µg/l in the flow-through test.

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*The reader is referred to the Guidelines for Deriving Water Quality Criteria for the Protection of Aquatic Life [43 FR 21506 (May 18, 1978) and 43 FR 29028 (July 5, 1978)] and the Methodology Document in order to better understand the following discussion and recommendation. The following tables contain the appropriate data that were found in the literature, and at the bottom of each table are the calculations for deriving various measures of toxicity as described in the Guidelines.

The bluegill has also been tested in static tests with unmeasured concentrations (U.S. EPA, 1978) and the adjusted 96-hour LC50 value is 24,400 µg/l. The geometric mean divided by the sensitivity factor results in the Final Fish Acute Value of 7,900 µg/l.

The data on acute static tests with the bluegill under comparable conditions (U.S. EPA, 1978) in this and other documents on structurally related chemicals show a correlation between toxicity and degree of chlorination. The 96-hour LC50 values for this species are 73,900 and 135,000 µg/l for 1,1- and 1,2-dichloroethylene, respectively, and 44,700 µg/l for trichloroethylene and 12,900 µg/l for tetrachloroethylene. These results indicate an increase in the lethal effect on bluegills with an increase in chlorine content. The correlation of toxicity for Daphnia magna is not as clear. The 48-hour LC50 values are 79,000, 85,200, and 17,700 µg/l for 1,1-dichloroethylene, trichloroethylene, and tetrachloroethylene, respectively.

The 48-hour EC50 value for Daphnia magna and trichloroethylene is 85,200 µg/l (U.S. EPA, 1978). After adjustment for static unmeasured concentrations the estimate is 72,200 µg/l, about 2.5 times higher than the fish LC50 values. Division by the sensitivity factor results in the Final Invertebrate Acute Value of 3,400 µg/l. Even though the LC50 value is higher than those for fish, the final value for invertebrate species is lower

because of the demonstrated greater range of species sensitivity of invertebrate species. The Final Invertebrate Acute Value of 3,400 µg/l becomes the Final Acute Value.

Chronic Toxicity

Only one chronic test has been conducted with freshwater organisms and trichloroethylene. That test with Daphnia magna provided incomplete results (U.S. EPA, 1978) because no adverse effects were detected at the highest test concentration of 10,000 µg/l. After adjusting the data for species sensitivity, the Final Invertebrate Chronic Value therefore would be greater than 2,000 µg/l.

Since the 48-hour EC50 value for Daphnia magna is 85,200 µg/l and there was no observed adverse effect during the chronic test at 10,000 µg/l, the difference between acute and chronic effects on this species is less than 8.5 times.

Residues

Bioconcentration by bluegill was studied (U.S. EPA, 1978) using radiolabeled trichloroethylene and after 14 days the bioconcentration factor was 17 (Table 4). The half-life of this compound in tissues was less than 1 day. Such bioconcentration and biological half-life data suggest no residue problem will occur at exposure concentrations that are not directly toxic to aquatic life.

Miscellaneous

After 96 hours there was a 50 percent loss of equilibrium among fathead minnows exposed to trichloroethylene at a concentration of 21,900 µg/l (Table 5). This effect occurred at a lower concentration than the lethal effects discussed previously (Table 1).

CRITERION FORMULATION

Freshwater - Aquatic Life

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value = 7,900 µg/l

Final Invertebrate Acute Value = 3,400 µg/l

Final Acute Value = 3,400 µg/l

Final Fish Chronic Value = not available

Final Invertebrate Chronic Value = greater than 2,000 µg/l

Final Plant Value = not available

Residue Limited Toxicant Concentration = not available

Final Chronic Value = greater than 2,000 µg/l

0.44 x Final Acute Value = 1,500 µg/l

The maximum concentration of trichloroethylene is the Final Acute Value of 3,400 µg/l and the 24-hour average concentration is the Final Chronic Value of 1,500 µg/l. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For trichloroethylene the criterion to protect freshwater aquatic life as derived using the Guidelines is 1,500 µg/l as a 24-hour average and the concentration should not exceed 3,400 µg/l at any time.

Table 1. Freshwater fish acute values for trichloroethylene

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Fathead minnow, Pimephales promelas	FT	M	96	40,700	40,700	Alexander, et al. 1978
Fathead minnow, Pimephales promelas	S	U	96	66,800	36,500	Alexander, et al. 1978
Bluegill, Lepomis macrochirus	S	U	96	44,700	24,400	U.S. EPA, 1978

* S = static, FT = flow-through

* U = unmeasured, M = measured

Geometric mean of adjusted values = 30,700 µg/l $\frac{30,700}{3.9}$ = 7,900 µg/l

Lowest value from a flow-through test with measured concentrations = 40,700 µg/l

Table 2. Freshwater invertebrate acute values for trichloroethylene (U.S. EPA, 1978)

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)
Cladoceran, Daphnia magna	S	U	48	85,200	72,200

* S = static

** U = unmeasured

Geometric mean of adjusted values = 72,200 µg/l $\frac{72,200}{21}$ = 3,400 µg/l

Table 3. Freshwater invertebrate chronic value for trichloroethylene (U.S. EPA, 1978)

Organism	Test*	Limits (ug/l)	Chronic Value (ug/l)
Cladoceran, *Daphnia magna*	LC	>10,000	>10,000

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* LC = life cycle or partial life cycle

Geometric mean of chronic values = >10,000 $\quad \frac{>10,000}{5.1}$ = >2,000 µg/l

Lowest chronic value = >10,000 µg/l

Table 4. Freshwater residues for trichloroethylene (U.S. EPA, 1978)

Organism	Bioconcentration Factor	Time (days)
Bluegill, *Lepomis macrochirus*	17	14

Table 5. Other freshwater data for trichloroethylene (Alexander, et al. 1978)

Organism	Test Duration	Effect	Result ug/l
Fathead minnow, Pimephales promelas	96 hrs	Loss of equilibrium EC50	21,900

SALTWATER ORGANISMS

Introduction

There are few data on the effects of trichloroethylene on saltwater organisms. There was a 50 percent decrease in ^{14}C uptake by the alga, Phaeodactylum tricornutum, at a concentration of 8,000 µg/l (Pearson and McConnell, 1975). Borthwick (1977) exposed sheepshead minnows and grass shrimp to 20,000 and 2,000 µg/l, respectively, and observed erratic swimming, uncontrolled movement, and loss of equilibrium after several minutes. No other data for saltwater organisms were found.

CRITERION FORMULATION

Saltwater - Aquatic Life

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value = not available

Final Invertebrate Acute Value = not available

Final Acute Value = not available

Final Fish Chronic Value = not available

Final Invertebrate Chronic Value = not available

Final Plant Value = not available

Residue Limited Toxicant Concentration = not available

Final Chronic Value = not available

0.44 x Final Acute Value = not available

No saltwater criterion can be derived for trichloroethylene using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available, and there are insufficient data to estimate a criterion using other procedures.

Table 6. Marine plant effects for trichloroethylene (Pearson & McConnell, 1975)

Organism	Effect	Concentration (ug/l)
Alga, *Phaeodactylum tricornutum*	50% decrease in uptake of ^{14}C during photosynthesis	8,000

Lowest plant value = 8,000 µg/l

Table 7. Other marine data for trichloroethylene (Borthwick, 1977)

Organism	Test Duration	Effect	Result (ug/l)
Sheepshead minnow, Cyprinodon variegatus	96 hrs	*	20,000
Grass shrimp, Palaemonetes pugio	96 hrs	*	2,000

*Intoxication for both fish and shrimp characterized by erratic swimming, uncontrolled movement, and loss of equilibrium after several minutes of exposure.

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Mammalian Toxicology and Human Health Effects

Exposure

Ingestion in Water. The National Organics Monitoring Survey observed trichloroethylene (TCE) in 4 of 112 drinking waters at a mean concentration of 11 µg/l in March-April 1976, in 28 of 113 cities averaging 21 µg/l in May-July 1976 and 19 of 105 cities averaging 1.3 µg/l in November - January 1977. TCE in waters may occur as a result of direct contamination or from atmospheric contamination by rainfall (Pearson and McConnell, 1975). TCE may also be formed during the chlorination of water (National Academy of Sciences, 1977; Bellar, et al. 1974).

Ingestion in Food. There is little information concerning the occurrence of TCE in foodstuffs. Because of its high partition coefficient (195/1) in an octanol water system, TCE is expected to bioaccumulate in fatty tissue. This has been borne out with a test exposure of bluegill fish which show a bioaccumulation factor of 17 for TCE relative to the water in the controlled test environment (U.S. EPA, 1978a). In England, TCE has been observed at concentrations up to 10 µg/kg in meats, and up to 5 µg/kg in fruits, vegetables and beverages (McConnell, et al. 1975). Packets of tea were found to contain 60 µg TCE/kg. Little TCE would be expected in other foodstuffs except in the case where TCE is used as a solvent for food extractions (Fishbein, 1976). Current maximum allowable concentrations of TCE in these foods are 10 mg/kg in instant coffee, 25 mg/kg in

ground coffee, and 30 mg/kg in spice extracts (Food and Drug Administration, 1974). Some manufacturers are now using trichloroethylene chloride rather than TCE for decaffeinating coffee (Waters, 1977). It is unlikely that significant exposures in the general population would be encountered by these sources because of the high volatility of TCE.

A bioconcentration factor (BCF) relates the concentration of a chemical in water to the concentration in aquatic organisms, but BCF's are not available for the edible portions of all four major groups of aquatic organisms consumed in the United States. Since data indicate that the BCF for lipid-soluble compounds is proportional to percent lipids, BCF's can be adjusted to edible portions using data on percent lipids and the amounts of various species consumed by Americans. A recent survey on fish and shellfish consumption in the United States (Cordle, et al. 1978) found that the per capita consumption is 18.7 g/day. From the data on the nineteen major species identified in the survey and data on the fat content of the edible portion of these species (Sidwell, et al. 1974), the relative consumption of the four major groups and the weighted average percent lipids for each group can be calculated:

Group	Consumption (Percent)	Weighted Percent Lipids
Freshwater fishes	12	4.8
Saltwater fishes	61	2.3
Saltwater molluscs	9	1.2
Saltwater decapods	18	1.2

Using the percentages for consumption and lipids for each of these groups, the weighted average percent lipids is 2.3 for consumed fish and shellfish.

A measured steady state bioconcentration factor of 17 was obtained for trichloroethylene using bluegills containing about one percent lipids (U.S. EPA, 1978). An adjustment factor of 2.3/1.0 = 2.3 can be used to adjust the measured BCF from the 1.0 percent lipids of the bluegill to the 2.3 percent lipids that is the weighted average for consumed fish and shellfish. Thus, the weighted average bioconcentration factor for trichloroethylene and the edible portion of all aquatic organisms consumed by Americans is calculated to be 17 x 2.3 = 39.

Inhalation. By far the most serious exposures of humans to TCE are confined to a relatively small industrial population (Fishbein, 1976). Currently the Threshold Limit Value (TLV)** adopted for TCE by the American Conference of Governmental Industrial Hygienists (ACGIH) is 535 mg/m^3 (100 ppm) (Am. Conf. Gov. Ind. Hyg. 1977).

Assuming a 10 m^3 tidal volume for an 8-hour day would result in a daily exposure of 5350 mg/day during the work week, which would greatly exceed that derived from food and water exposures under ordinary circumstances. Other inhalation exposures would be associated with the use of products containing TCE, such as cleaning fluids (Waters, et al. 1977). There are insufficient data to make a quantitative assessment of exposure from such

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**Threshold limit values adopted for TCE by the American Conference of Governmental Industrial Hygienists (ACGIH) refer to airborne concentrations of substances and represent conditions under which it is believed that nearly all workers may be repeatedly exposed day after day without adverse effect. Because of wide variations in individual susceptibility, however, a small percentage of workers may experience discomfort from some substances at concentrations at or below the threshold limit; a small percentage may be affected more seriously by aggravation of a pre-existing condition or by development of an occupational illness." (American Conference of Governmental Industrial Hygiensits 1977).

products. The hazards of such exposure would more often be acute because of their sporadic use rather than longterm as in the industrial setting.

A problem encountered with the use of TCE as an anesthetic (Defalque, 1961), and in certain industrial circumstances where the liquid or vapor may come into contact with hot surfaces or be exposed to ultraviolet radiation (as from inert gas metal arc welding) (Rinzema, 1971), is the formation of breakdown products with high degrees of toxicity, such as phosgene and dichloroacetylene (Goodman and Gilman, 1966). The occurrence of such compounds complicates epidemiological assessments of TCE effects in the workplace.

Dermal. Stewart and Dodd (1964) conducted controlled human studies from which they concluded that skin exposure is insignificant relative to inhalation exposure and that, during normal industrial use, there is little likelihood that toxic amounts of TCE will be absorbed through the skin. It seems reasonable to conclude that dermal absorption could make little additional contribution to that obtained through either inhalation or ingestion.

Pharmacokinetics

Absorption. TCE is readily absorbed by all routes of exposure. This would be predicted upon the basis of its physical and chemical properties (Goldstein, et al. 1974). Most human

data concerning TCE absorption has been obtained with inhalation as the route of exposure because of interest in the compound as an industrial toxicant and its use as an anesthetic. Stewart, et al. (1962) reported TCE concentrations of 4.5 to 7 mg/l of blood within 2 hours of exposing volunteers to a time weighted average concentration of 1420 mg/m^3 (range: 856-2140 mg/m^3) Concentrations did not rise further with time implying a rapid approach to steady-state with inhalation exposures. Retention of inhaled TCE has been estimated to approximate 36 percent by Nomiyama and Nomiyama (1971) and 37 to 41 percent by Monster, et al. (1976).

Absorption of TCE following ingestion has not been studied in humans. In rats, 72 to 85 percent and 10 to 20 percent of the total orally administered dose could be accounted for in expired air and urine, respectively, with less than 0.5 percent appearing in the feces (Daniel, 1963). This indicates that at least 80 percent (and probably more) of ingested TCE is systemically absorbed.

Stewart and Dodd (1964) detected up to 2.7 mg/m^3 TCE in alveolar air following immersion of an individual's thumb in TCE for 30 minutes. Although the data is insufficient to calculate rate of absorption through the skin, it does demonstrate rapid absorption of TCE through intact human skin.

Distribution. The distribution of TCE in the body is what would be expected on the basis of its chemical and physical properties (Goldstein, et al. 1974). Based on its partition

coefficient of 195 to 1 in an octanol/ water system (log P = 2.29), TCE is expected to bioaccumulate slightly in fatty tissue. Tables 8 and 9 show the distribution of TCE in various tissues as compared to fat as observed both in man (McConnell, et al. 1975) and animals (Fabre and Truhaut, 1952). In guinea pigs almost equivalent concentrations are observed in the adrenals: ovaries tend to be about 50 percent and other tissues about 25 percent the concentration observed in fat (Table 9).

Laham (1970) demonstrated transplacental diffusion of TCE in humans. The ratio of fetal blood concentrations to maternal blood concentrations varied between 0.52 and 1.90.

Table 8. Concentration of TCE in human tissues at autopsy (McConnell, et al. 1975)

Subject	Age/Sex	Tissues	Concentration (µg/kg wet tissue)
A	76/F	Body fat	32
		Kidney	41
		Liver	5
		Brain	1
B	76/F	Body fat	2
		Kidney	3
		Liver	2
		Brain	41
C	82/F	Body fat	1.4
		Liver	3.2
D	48/M	Body fat	6.4
		Liver	3.5
E	65/M	Body fat	3.4
		Liver	5.2
F	75/M	Body fat	14.1
		Liver	5.8
G	66/M	Body fat	4.6
H	74/F	Body fat	4.9

Table 9. Distribution of TCE in guinea pigs (Fabre and Truhaut, 1952)

	Concentration (mg/100 g fresh tissue)			
Organ	TCE(1)	TCE(2)	TCE(3)	TCE(4)
Adrenals	-	3.4	2.2	3.8
Blood	1.3	1.0	0.5	0.8
Brain	0.5	0.7	0.9	1.0
Fat	3.1	3.5	3.9	3.8
Kidney	2.2	0.8	1.4	1.8
Liver	0.8	0.5	1.0	0.6
Lungs	0.8	1.2	0.7	0.8
Muscle	-	0.5	0.2	0.2
Ovaries	-	2.3	2.3	-
Spleen	1.7	1.9	1.3	0.9
Urine	-	3.5	3.1	2.6

(1) Inhalation of 9 mg/liter, 4 hr daily for 5 days; total 20 hr.

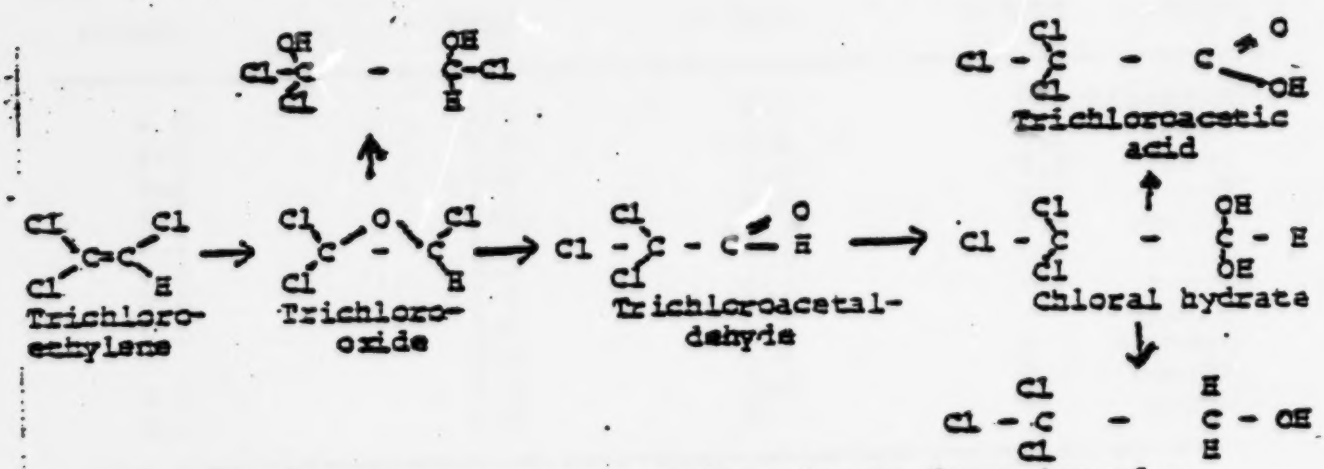
(2) Inhalation of 6 mg/liter, 4.5 hr daily for 13 days; total 58.5 hr.

(3) Inhalation of 6 mg/liter, 5 hr daily for 19 days, total 95 hr.

(4) Inhalation of 7 mg/liter, 5 hr daily for 23 days; total 115 hr.

Metabolism. The metabolism of TCE appears to be central to its long-term deleterious effects. In a qualitative sense, metabolism of TCE appears similar across species (Ikeda and Ohtsuji, 1972; Kimmerle and Eben, 1973 a, b). The principal products of TCE metabolism measured in urine are trichloroacetaldehyde, trichloroethanol and trichloroacetic acid, and conjugated derivatives (glucuronides) of trichloroethanol. The metabolite trichloroethanol has been suggested as responsible for long-term CNS effects of TCE inhalation (Ertle, et al. 1972). In terms of reported carcinogenic and mutagenic effects of TCE, intermediary metabolites rather than the final products of the

pathway are of paramount importance. Daniel (1963) suggested the following pathway for TCE metabolism:



The essential feature of this pathway is the formation of a reactive epoxide, trichloroethylene oxide, which can alkylate nucleic acids and proteins (Van Duuren and Banerjee, 1976; Bolt and Filser, 1977). Such covalent binding can be increased with epoxide hydrase inhibition (Van Duuren and Banerjee, 1976). As can be seen, the formation of trichloroacetaldehyde (Byington and Leibman, 1965) requires rearrangement of chlorine atoms (Henschler, 1977). The measurement of specific activities of trichloroacetic acid and trichloroethanol following oral administration to rats of radiolabelled TCE indicates that this rearrangement is intramolecular and not an exchange with the body chloride pool (Daniel, 1963). The importance of this observation is that it is not observed with thermal rearrangements in vitro (Greim, et al. 1975). Although urinary excretion of trichloroethanol precedes excretion of trichloroacetic acid following exposure, it is clear that this is not a precursor-product relationship since trichloroethanol is poorly converted

to trichloroacetic acid in vivo (Daniel, 1963). Rather the earlier and more extensive excretion of trichloroethanol appears to result from a more rapid conversion of trichloroacetaldehyde to trichloroethanol than its conversion to trichloroacetic acid (Ikeda and Imamura, 1973).

There is one report that the pattern of metabolism of TCE in humans differs between male and female (Nomiyama and Nomiyama, 1971). Within the first 24 hours of exposure to 1345-2044 mg/m^3 in air, females tend to excrete more trichloroacetic acid and less trichloroethanol than males. Similarly, the ratio between trichloroethylene exposure and urinary trichloroacetic acid excretion appears to decrease with age (Grandjean, et al. 1955). These data would suggest the possibility of age and sex differences in susceptibility to the adverse effects of TCE.

Phenobarbital administration to rats or hamsters in vivo increases the oxidation of TCE. This results in an increase in the conversion of trichloroethylene to trichloroacetaldehyde (Ikeda and Imamura, 1973). No differences were observed in the conversion of trichloroacetaldehyde to trichloroacetic acid or trichloroethanol. Despite induction of microsomal enzymes, conversion of TCE to trichloroacetaldehyde appears to remain as the rate limiting step. As predicted by the increased activity of alcohol dehydrogenase (Friedman and Cooper, 1960) the total trichloroethanol excretion is increased to a greater extent than trichloroacetic acid excretion by phenobarbital pretreatment (Leibman and McAllister, 1967). It is notable that oxidation of

trichloroethylene is reduced effectively by the alcohol dehydrogenase inhibitor tetraethyl-thiuram disulfide (Disulfuram) (Bartonicek and Teisinger, 1962). Muller, et al. (1975) observed blood levels of TCE in volunteers inhaling TCE and concurrently ingesting ethanol to be 2 1/2 times higher than in the absence of ethanol: the TCE level in brain can be expected to exhibit an equivalent increase. These authors suggest that this accumulation of TCE (postulated to result from complete depression by ethanol of TCE oxidation) may be responsible for the ethanol intolerance observed in workers exposed to TCE. On the other hand, Ertle, et al. (1972) believe formation and accumulation of trichloroethanol to be responsible for the "psycho-organic syndrome" encountered during occupational exposure to TCE. Trichloroethanol is said to be at least three times more potent than TCE on a variety of measures of central nervous system activity (Mikiskova and Mikiska, 1966). Ethanol has been shown to increase the rate of reduction of chloral hydrate to trichloroethanol in humans (Sellers, et al. 1971) and experimental animals (Gessner, 1973; Kaplan, et al. 1968), thus an alternative explanation to that of Muller, et al. is offered for TCE-ethanol interactions. If trichloroethanol is the agent responsible for chronic central nervous system toxicity, inducers of microsomal enzymes in general might be expected to have a synergistic effect on the toxicity of TCE. The study of the effect of microsomal induction on hepatoxicity has not yielded consistent results across laboratories (Cornish, et al. 1973; Carlson, 1974; Moslen, et al. 1977a). The differences in these results appear to be attributable to different modes of adminis-

tration of TCE. Inhalation of 1 percent (v/v) in air resulted in increased hepatotoxicity subsequent to phenobarbital pretreatment whereas the effects of intraperitoneal injections of up to 2 ml TCE/kg were not enhanced by such pretreatment. These results may be complicated by the fact that high doses of TCE deactivate microsomal enzyme systems (Moslen, et al. 1977a).

Excretion. The biological half-life of TCE and its metabolites has been examined in humans and experimental animals. In the rat (male, SPF-Wistar II), concentrations of TCE in expired air were undetectable 8 hours after inhalation of TCE at concentrations of up to 330 ppm (Kimmerle and Eben, 1973a). After administration by stomach tube of ^{36}Cl-labelled TCE to Wistar rats, 72 to 85 percent of the radioactivity (presumably primarily TCE) was recovered in the exposed air with a half-life of 5 hours (Daniel, 1963). In humans, inhaled TCE is rapidly absorbed from the lungs, with 50 to 70 percent being retained and metabolized in the body. Four hours after acute exposure to approximately 215 mg/m^3 TCE was undetectable in the blood. On the other hand, trichloroethanol, a major metabolite, persisted in blood for several hours. TCE and its metabolites are excreted in exhaled air, urine, sweat, feces and saliva (Kimmerle and Eben, 1976). TCE is lost from the body with a half-time of about 1 1/2 hours (Stewart, et al. 1962). Trichloroacetic acid, trichloroethanol and the glucuronide of trichloroethanol are excreted more slowly. The biological half-life measured in urine

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in humans has ranged from 12 to 50 hours for trichloroethanol and 36 to 73 hours for trichloroacetic acid (Ikeda and Imamura,

1973; Ertle, et al. 1972). Excretion of trichloroethanol and its glucuronide increase linearly with exposure to TCE. However, the rate of excretion of trichloroacetic acid increases linearly with inhalation exposures up to 268 mg/m^3 but tends to level out with higher exposures in humans (Ikeda and Imamura, 1973). These data in humans are consistent with kinetics of conversions of trichloroacetaldehyde to trichloroethanol and trichloroacetic acid in rats (Ikeda and Imamura, 1973).

Effects

Toxicity. Classically, TCE is known as a central nervous system depressant. In fact, the compound has been used medically as a general anesthetic (Defalque, 1961). However, its use has declined because of impurities formed on contact with soda lime used as an absorbent for carbon dioxide. Dichloroacetylene, one of the compounds formed, produces cranial nerve palsies (Goodman and Gilman, 1966).

Although the clinical picture is predominated by the direct CNS depression produced by high exposures to TCE, there is evidence of longer term CNS effects resulting from TCE exposure (Grandjean, et al. 1955). There is some justification for suspecting that these effects may arise from metabolites of TCE. Chloral hydrate and trichloroethanol are metabolites known to affect the nervous system (Ertle, et al. 1972). As chloral hydrate does not ordinarily accumulate with TCE exposures (Leibman and McAllister, 1967; Cole, et al. 1975) and because of

the greater nervous system activity of trichloroethanol (Cabana and Gessner, 1970; Krieglstein and Stock, 1973), the latter compound has been implicated as being responsible for the longer term CNS effects of TCE.

Psychomotor function and subjective responses to TCE have been studied in short-term, controlled human clinical studies. Stewart, et al. (1970) reported mild fatigue and sleepiness in normal adults after 4 to 5 days of exposure to 1,070 mg/m^3 for 7 hours a day. Stopps and McLaughlin (1976) observed a progressive decline in psychomotor function of one adult male at concentrations of TCE of 1,070 mg/m^3 and up for a period of less than 3 hours. In a larger study involving six male students exposed to two 4-hour exposures in one day at an average concentration of 590 mg/m^3 TCE, Salvini, et al. (1971) demonstrated a statistically significant decrease in performance ability. Nomiyama and Nomiyama (1977) reported headaches in healthy male students exposed to 433 mg/m^3 for 4 hours a day for 6 days, but were unable to demonstrate effects on a flicker fusion test or two point discrimination even at 1,070 mg/m^3. These studies, however, are of such short duration that they are measuring primarily the threshold for the general central nervous system depressant activities of TCE. They are of little value in assessing the possibility of longer term cumulative and perhaps irreversible effects on nervous system function which have been suggested by epidemiological studies (Grandjean, et al. 1955; Nomiyama and Nomiyama, 1977). They do suggest, however, that the TLV for TCE (535 mg/m^3) has been established very close to the

threshold for the acute effects of TCE on healthy adult male volunteers.

In an epidemiological study, Grandjean, et al. (1955) obtained evidence of increased nervous system disorders in occupational exposures of 5 to 15 years duration at concentrations measured at the time of the study that averaged below the TLV. Nomiyama and Nomiyama (1977) also report headaches in workers exposed to as little as 144 mg/m^3. Bardodej and Vyskoch (1956) reported insomnia, tremors, severe neuroasthemic syndromes coupled with anxiety states, and bradycardia that increased in frequency with length of occupational exposure to levels of TCE ranging from 160 to 3,400 mg/m^3 Disturbances of the nervous system were reported to continue for up to at least one year after final exposure. Such studies have inherent problems in relating such effects directly to TCE because of the lack of historical data and the impossibility of ruling out contaminants or breakdown products. However, questions raised by these data have not been adequately addressed in controlled studies in humans or experimental animals.

TCE also carries some abuse potential, in that cases of deliberate and repetitive inhalation have been documented (James, 1963; Ikeda and Inamura, 1973). In occupational settings, this abuse has resulted in inability to sleep on off-days without inhalation of TCE (Bardodej and Vyskoch, 1956). TCE abuse has been associated with hepatorenal toxicity (Clearfield, 1970).

Death in acute overwhelming inhalation exposure is most commonly due to respiratory and cardiac failure (Smith, 1966).

Studies of effects of TCE on the nervous system of experimental animals have been extremely limited, confined to behavioral and histopathological studies. Behavioral studies have generally confirmed the CNS depressant activity of TCE observed in man at roughly equivalent exposures in rats (Khorvat and Formanek, 1959; Goldberg, et al. 1964a, b). Such effects appear reversible after 3 to 4 weeks exposure of rats to average concentrations of 670 mg/m^3 for 4 hours a day, 5 days a week (Goldberg, et al. 1964b). Bartonicek and Brun (1970), at doses of TCE ranging from 144 to 333 mg/kg of body weight per day in the rabbit by intramuscular injection demonstrated loss of Purkinje cells and associated basket cells in the cerebellum and other less specific damage to the telencephalic cortex, basal ganglia and brain stem nuclei. Similar alterations had been demonstrated by Bernardi, et al. (1956) with inhalation exposures to 9,630 mg/m^3 for 20 to 30 days in rabbits and 1,600 to 2,700 mg/m in dogs (Baker, 1958). Evidence of such permanent damage has been reported only with high doses for relatively short periods of time. As mentioned above, the long-term, low dose effects of TCE on the central nervous system have not been well-evaluated.

Prolonged occupational exposures to TCE have been associated with impairment of the peripheral nervous system. Persistent neuritis (Bardodej and Vyskoch, 1956), and temporary loss of

tactile sense, and paralysis of the fingers which come into direct contact with the solvent have been reported (McSirney, 1954).

Use of TCE as an anesthetic has been associated with toxicity to a number of other organ systems. This literature was reviewed by Defalque (1961). Cardiac arrhythmias including bradycardia, auricular and ventricular premature contractions and ventricular extrasystoles have been reported. The dose-response relationship for these effects has not been established in man or experimental animals.

Fatal hepatic failure has been observed following use of TCE as an anesthetic. Such failure generally has involved patients with complicating diseases such as malnutrition, toxemias, and burns, or who had received transfusions (Defalque, 1961). Liver failure in experimental animals is marked by generalized binding of TCE metabolites to proteins and nucleic acids (Bolt and Filser, 1977). In contrast to vinyl chloride, binding of TCE metabolites appears to involve binding to free amino groups as well as to sulfhydryl groups. Binding of TCE metabolites and its hepatoxic effects has been reported to increase with induction of microsomal mixed function oxidases (MFO) and treatment with 1,2-epoxy-3,3,3-trichloropropane, an inhibitor of epoxide hydrase. These findings are somewhat complicated by the fact that liver necrosis and reduction in liver glutathione were not acutely produced by inhaled TCE without pretreatment with phenobarbital (Adams, et al. 1951; Moslen, et al. 1977b). Glutathione

conjugates are not identified metabolites of TCE, although they have been suggested (Reynolds and Moslen, 1977). Glutathione acts to protect against oxidative damage to tissues (DeBruin, 1976). This makes it difficult to rationalize TCE hepatotoxicity resulting simply from increased rates of metabolism, in that a scavenging role for glutathione cannot be invoked as a protective mechanism as it can be for chloroform (Docks and Krishna, 1976). It is possible that the decreased glutathione represents increased peroxidative activity with combined phenobarbital and TCE treatment (Ullrich, 1975). On the other hand, increased serum glutamate-oxalacetate transaminase activities (also indicative of hepatotoxicity) may be induced by injected TCE, but the effect is not enhanced by phenobarbital pretreatment (Cornish, et al. 1973). Despite these reports in using high doses in experimental animals and in humans exposed to anesthetic doses of TCE, liver damage in the industrial setting appears to be rare (Bardodej and Vyskoch, 1956), and difficult to produce in experimental animals with acute sub-anesthetic doses in animals for up to 8 weeks (Kylin, et al. 1963). Even longer term exposures of up to 17,000 mg/m^3 failed to produce more than a low incidence of fatty infiltration of the liver (Kylin, et al. 1965). However, hepatic damage is observed in cases of repeated abuse of TCE (Huff, 1971).

Renal failure has been an uncommon problem with TCE anesthesia (Defalque, 1961). Although depressed kidney function can be documented with TCE in experimental animals, it requires very high doses (Klaasen and Plaa, 1967) and on a relative basis

is much less potent than chloroform or carbon tetrachloride. Renal damage has been reported in fatal cases involving TCE abuse (Huff, 1971).

Industrial use of TCE is often associated with dermatological problems (Bauer and Rabens, 1974). Most often this is associated with skin contact directly with concentrated solvents and is probably limited to effects secondary to solvent action. No such effects have been reported with TCE in dilute aqueous solutions.

TCE, along with a number of other low molecular weight chlorinated compounds, greatly increases bile duct-pancreatic fluid flow in rats (Hamada and Peterson, 1977). The fluid is considerably altered in protein and in ionic composition. The physiological significance of this alteration is presently unknown.

Synergism and/or Antagonism. Long-term toxicity of TCE appears to depend largely on its metabolic products. Consequently, second chemicals which enhance or inhibit steps in the metabolism of TCE will act to either increase or decrease its toxicity. Many drugs (e.g., phenobarbital) and environmental chemicals (e.g., PCB) induce the mixed function oxidase. These compounds have in some studies been observed to act synergistically with TCE in producing liver damage (Carlson, 1974; Moslen, et al. 1977 Reynolds and Moslen, 1977). Rats exposed to 37,000, 42,000, and 56,000 mg/m^3 respectively, TCE vapors for 2 hours showed elevated activities of serum glutamic

pyruvic transaminase, glutamic oxaloacetic transaminase, and isocitrate dehydrogenase. Hepatotoxicity, as indicated by these increases of hepatic enzymes in the serum, was greatly enhanced by pretreatment with the metabolic inducers phenobarbital and 3-methylcholanthrene (Carlson, 1974). The latter finding suggests that a metabolite of TCE contributes to the toxicity of this compound. Metabolism of TCE shares some common enzymatic steps with the metabolism of ethanol. While TCE inhibits oxidation of ethanol, ethanol appears to enhance formation of trichloroethanol (Gessner, 1973; Cabana and Gessner, 1970). Enhanced toxicity of TCE and its metabolic products has been observed with ethanol ingestion in both man (Bardodej and Vyskoch, 1956; Seage and Burns, 1971) and experimental animals (Cornish and Adefunin, 1966; Ferguson and Vernon, 1970; Gessner and Cabana, 1970).

TCE has also been reported to sensitize the myocardium to arrhythmias induced by epinephrine (Dhuner, et al. 1957). This has been observed to occur after accidental ingestion of TCE as well and has proven fatal in some cases (Defalque, 1961). Since chloral hydrate-associated arrhythmias have been reversed by b-adrenergic blocking agent, these activities may be associated with metabolites of TCE (DiGiovanni, 1969).

The central nervous system depressant activity of TCE would be at least additive with the effects of other central nervous system depressants and generally antagonistic towards stimulants (Defalque, 1961). However, the latter would be primarily

symptomatic antagonists having little relationship to underlying toxicity of the compound, particularly long-term toxicity.

Chloral hydrate has been reported to enhance the anticoagulant effects of warfarin (Koch-Weser and Sellers, et al., 1971) and bishydroxycoumarin (Belles and Foster, 1974). The potentiation is apparently associated with a displacement of the anticoagulants from plasma albumin by trichloroacetic acid (Sellers and Koch-Weser, 1970), as evidenced by a shortened warfarin half-life. Many other drugs bind to albumin and could be displaced by trichloroacetic acid resulting in a potentiation of their usual pharmacological properties (Ertle, et al. 1972). As pointed out earlier, trichloroacetic acid is a metabolite of TCE as well. Consequently, TCE exposures have the potential of synergizing the effects of anticoagulant drugs.

Teratogenicity. Although it has been suggested that mutagenic agents should be considered teratogens, this has not yet been borne out with TCE. Exposure of mice and rats to 1600 mg/m³ TCE on days 6 through 15 of gestation for 7 hours a day did not produce teratogenic effects in mice or rats (Schwetz, et al. 1975). Although not statistically significant, there was evidence of hemorrhages in the cerebral ventricles (2/12 litters) and cases of undescended testicles (2/12 litters) observed in the TCE treated mice that were observed at very low incidence or not at all in other groups (1/90 otherwise treated or control litters for hemorrhage in cerebral ventricles, 0/90 for undescended

testicles). This appears to be the only teratogenesis study conducted with TCE.

Mutagenicity. TCE has been reported to possess mutagenic activity in a number of bacterial strains. Greim, et al. (1975) demonstrated reverse mutations in E-coli K12 when coupled in vitro with phenobarbital-induced mouse liver microsomes at a concentration of 3.3 mM (434,000 µg/l) in the incubation media. The highest mutation frequency (2.32 times spontaneous mutation rate) was seen in the arg^{+} back mutation system. Simmon, et al (1977) found that in the presence of Aroclor 1254 induced sprague Dawley rat liver microsomes or B6-C3-F1 mouse liver microsomes, 6mM to 22 mM (789,091 µg/l to 2,893,333 µg/l), TCE exposure in a dessicator increased the S. typhimurium (TA100) revertant rate. Similar observations have been made in the yeast Saccharomyces cerevisiae (Strain XV 185-14C) in the presence of metabolizing mouse liver microsomes. Concentrations of 10 µl/ml and 20 µl/ml (14.5 g/l to 29 g/l) significantly increased the frequency of homoserine, histidine, and lysine revertants over those of control levels after one to four hours of exposure (Shahin and von Barstel, 1977). TCE has been uniformly negative in mutagenicity testing in the absence of metabolic activation (Simmon, et al. 1977; Greim, et al., 1945; Shahin and von Barstel, 1977). Henschler (1977) and his associates have closely associated the mutagenic activity of the chlorinated ethylenes with unsymmetrical chlorine substitution that renders the respective epoxides unstable (e.g. vinyl chloride, 1,1-dichloroethylene and trichloroethylene). There is some doubt as

to the mutagenicity of TCE. On chemical analysis, technical grade TCE was found to contain epichlorohydrin and epoxibutane, two compounds that Henschler, et al. (1977) observed to be more potent mutagens than TCE in S. typhimurium (TA 100). Pure TCE was weakly mutagenic. These investigators concluded that the mutagenic activity formerly attributable to TCE probably was due in part to mutagenic contaminants, found in some samples of TCE.

Carcinogenicity. Trichloroethylene has been shown to induce transformation in a highly sensitive in vitro Fischer rat embryo cell system (F1706) that is used for identifying carcinogens. At a concentration of 1M, TCE induced transformation of rat embryo cells as characterized by the appearance of progressively growing foci made up of cells lacking contact inhibition and by the growth of macroscopic foci when inoculated in semi- solid agar. The transformed cells grew as undifferentiated fibrosarcomas at the site of inoculation in 100 percent of newborn Fischer rats between 27 and 68 days post-inoculation (Price, et al. 1978).

The National Cancer Institute (NCI) (1976) observed increased incidence of hepatocellular carcinoma in mice (strain B6C3-F1) treated with TCE. The time weighted doses administered for 5 days/week for 78 weeks were 1,169 and 2,339 mg/kg for males and 869 and 1,739 mg/kg for females. Similar experiments in Osborne-Mendel rats failed to increase the incidence of tumors in this species. However, the rats also responded poorly to the positive control carbon tetrachloride, indicating the B6C3-F1 mouse to be a much more sensitive test animal to induction of carcinomas by

chlorinated compounds. The data obtained from mice are summarized in Table 10. Some evidence of metastasis of hepatocellular carcinomas to lung was observed in both low and high dose male mice (4/50 and 3/48, respectively).

Table 10. Incidence of hepatocellular carcinoma in TCE-treated B6C3-F1 mice (NCI, 1976)

	Males	Females
Control	1/20	0/20
Low dose	26/50	4/50
High dose	31/48	11/47

It has been pointed out that TCE used in the NCI bioassay (1976) contained traces of monofunctional alkylating agents, epichlorohydrin and epoxibutane as stabilizers (Henschler et al., 1977). The mutagenic potency of these compounds in Salmonella TA100 was of sufficient magnitude to suggest that they might account for the observed carcinogenicity of TCE. However, as the grade of TCE used experimentally was representative of that used industrially, any contamination of drinking water by TCE would probably be of similar quality. Consequently, the results of the NCI bioassay have been accepted for the purposes of this document.

Only one systematic study of trichloroethylene exposure and the incidence of human cancer seem to be available (Axelson, et al. 1978). Workers were segregated on the basis of trichloroacetic acid concentrations in the urine, which would indicate time-weighted exposures of more or less than 160 mg

TCE/m^3 and on the basis of more or less than 10 years exposure. A total of 518 men were included in the study, but only eight fell into the latter category. In no category was any excess cancer mortality observed. However the authors note that "only a very strong effect of TCE with regard to liver carcinogenicity would have been detectable with the size of this study" and conclude that, although the cancer risk to man cannot be ruled out, exposure to low levels of TCE probably does not present a very serious and general cancer hazard.

CRITERION FORMULATION

Existing Guidelines and Standards

Trichloroethylene has been regulated primarily from the industrial health standpoint. Concentrations allowed in the working environment very widely in different countries (Table 14). Because of use of TCE in decaffeintaing coffee and the extraction of spice oleoresins, the Food and Drug Administration has limited concentrations of TCE that may be allowed in the final product. These limits are 10 mg/kg in instant coffee, 25 mg/kg in ground coffee and 30 mg/kg in spice extracts (Food and Drug Administration, 1974).

TABLE 14

Industrial hygiene standards for trichloroethylene in various countries (Fishbein, 1970)

	mg/m^3	Calculated Allowable daily exposure mg/day
USA	535	3821
Sweden	160	1143
Czechoslovakia	250	1786
Federal Republic of Germany	260	1857
German Democratic Republic	250	1768
USSR	1	7

The presently established American Conference of Governmental Industrial Hygienists (ACGIH) TLV listed in Table 11 (in the document), has been established entirely on the basis of short-term exposures of healthy male volunteers. This level has not taken into account the possibility of potential synergists present in the general environment or the possibility of sensitive populations (American Conference

of Governmental Industrial Hygienists, 1977). It has not yet incorporated consideration of TCE carcinogenicity indicated by recent NCI data (1976). As can be seen in the table above, industrial hygiene standards established by European countries are less than 1/2 that allowed in the U.S.

Basis and Derivation of Criterion

No quantitative animal or human data exist that may be used to refine the AGCIH estimate of non-carcinogenic risks from exposure to TCE. Sensitive populations undoubtedly exist, as documented by interactions of TCE toxicity with ethanol. However, no quantitative data exist on which to weigh such factors. Calculation of an acceptable concentration for water quality criteria from the TLV on the basis proposed by Stokinger and Woodward (1958) is illustrated below:

$$\frac{535\ mg/m^3 \times 50\ m^3/week \times 0.36^*}{7\ days/week \times 100^{**}} = 14\ mg/day$$

*Coefficient of respiratory absorption vs. absorption via ingestion.

**Safety factor for sensitive populations.

Assuming a 2 liter daily consumption of water and a safety factor of 100 for sensitive populations and the consumption of 18.7 grams of fish which has a bioconcentration factor of 39 concentrations of TCE in drinking water would be limited to 5.13 mg/liter on this basis.

Under the Consent Decree in NRDC v. Train, criteria are to state "recommended maximum permissible concentrations (including where appropriate, zero) consistent with the protection of aquatic organisms, human health, and recreational activities." Trichloroethylene is suspected of being a human carcinogen. Because there is no recognized safe concentration for a human carcinogen, the recommended concentration of trichloroethylene in water for maximum protection of human health is zero.

Because attaining a zero concentration level may be infeasible in some cases and in order to assist the Agency and States in the possible future development of water quality regulations, the concentrations of trichloroethylene corresponding to several incremental lifetime cancer risk levels have been estimated. A cancer risk level provides an estimate of the additional incidence of cancer that may be expected in an exposed population. A risk of 10^{-5} for example, indicates a probability of one additional case of cancer for every 100,000 people exposed, a risk of 10^{-6} indicates one additional case of cancer for every million people exposed, and so forth.

In the Federal Register notice of availability of draft ambient water quality criteria, EPA stated that it is considering setting criteria at an interim target risk level of 10^{-5}, 10^{-6}, or 10^{-7} as shown in the table below.

Exposure Assumptions (per day)	Risk Levels and Corresponding Criteria (1)			
	0	10^{-7}	10^{-6}	10^{-5}
2 liters of drinking water and consumption of 18.7 grams fish and shellfish. (2)	0	0.21 µg/l	2.1 µg/l	21 µg/l
Consumption of fish and shellfish only.	0	0.78 µg/l	7.8 µg/l	78 µg/l

(1) Calculated by applying a modified "one-hit" extrapolation model described in the Methodology Document to the animal bioassay data presented in Appendix I and in Table 10. Since the extrapolation model is linear at low doses, the additional lifetime risk is directly proportional to the water concentration. Therefore, water concentrations corresponding to other risk levels can be derived by multiplying or dividing one of the risk levels and corresponding water concentrations shown in the table by factors such as 10, 100, 1,000, and so forth.

(2) Approximately 27 percent of the trichloroethylene exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of 39-fold. The remaining 73 percent of trichloroethylene exposure results from drinking water.

Concentration levels were derived assuming a lifetime exposure to various amounts of trichloroethylene, (1) occurring from the consumption of both drinking water and aquatic life grown in waters containing the corresponding trichloroethylene concentrations and, (2) occurring solely from consumption of aquatic life grown in the waters containing the corresponding trichloroethylene concentrations. Because data indicating other sources of trichloroethylene exposure and their contributions to total body burden are inadequate for quantitative use, the figures reflect the incremental risks associated with the indicated routes only.

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APPENDIX I

Derivation of Criterion for Trichloroethylene

The NCI bioassay with male mice at an average dose, administered by stomach tube of 1,169 mg/kg administered 5 times per week for 78 weeks is used. The experiment was terminated after 90 weeks. In matched control animals the incidence of heptocellular carcinoma was 1/20 and in treated animals it was 26/50. The fish bioaccumulation factor is 39. The parameters of the extrapolation model are:

nt = 26	le = 78 weeks
NT = 50	d = 1169 x 5/7 = 835 mg/kg/day
nc = 1	w = 0.034 kg
NC = 20	L = 90 weeks
Le = 90 weeks	R = 39

The result is that the water concentration should be less than 21 µg/l (21.47 µg/l) in order to keep the individual lifetime risk below 10^{-5}.